OUTLINE OF THE PROPOSED WORK FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN PHARMACEUTICAL SCIENCES

Submitted To

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Topic

Nanoparticals -A novel approach in improvement of pharmacokinetic profile of Indian origin polyherbal antidiabetic formulations.

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AIM & OBJECTIVE:

The present study aims to design a novel drug delivery system of antidiabetic herbal drugs which improves the pharmacokinetic profile of antidiabetic herbal drugs. The objectives of present study are as below

1. Use the current scientific literature to identify potential target compounds.
2. Extraction of plant material using proper solvent.
3. To use the current scientific literature to identify potential target compounds.
4. To evaluate in vitro antidiabetic activity of extracts.
5. Preparation of nanoparticals of prepared drug extracts.
6. Evaluation of pharmacokinetic profile of prepared dosage form.
7. Bioequivalence study of prepared drug delivery system with marketed preparation.

INTRODUCTION:

Diabetes is a chronic metabolic disorder that affects millions of people worldwide and takes a heavy toll on human life. Diabetes mellitus a well known endocrine disorder and it is most common in India now a day. The reason may be life style and genetic factors. Due these factors the diabetic monocytes produce increased superoxide anion. In premature atherosclerosis and oxidative stress patient's diabetes is a major risk factor. Diabetes is a disorder indicating insufficient insulin production or increasing resistance to its performance. Chemical agents are used generally to treat this upsetting disease but herbal treatments for diabetes having good effect in patients with insulin dependent and non-insulin-dependent diabetes, diabetic retinopathy, diabetic peripheral neuropathy, etc. Diabetes is rapidly influencing the world population and especially type 2 diabetes with 90-95% occurrence resulting from impaired insulin production or consumption whereas World Health Organization estimated that it might affect the 300 million or more population till 2025. Many oral hypoglycemic agents like biguanides, glinides and sulfonylureas are in use today to manage diabetes but they possess adverse side effects, so the research is focused mostly on the discovery of safer antidiabetic agents. Over the centuries, herbal drugs have served as a major source of medicines for the prevention and treatment of diseases including diabetes mellitus. There are more than 200 species of plants exhibit hypoglycemic properties. Treatment of diabetics often poses a problem in selection of the proper drug, its dose and unwanted side effects. Therefore, newer drugs with the least side effects but with highest efficiency are being relentlessly searched for.[1]

In recent years, nanotechnology has given new hope for the formulation of various drugs against a myriad of diseases, including diabetes. The strategy of applying nanotechnology to plant extracts has been widely cited in the literature, because nano-structured systems could potentiate action of plant extracts, promote sustained release of active constituents, reduce the required dose, low toxicity, decrease side effects, and improve activity. Moreover, several studies have been used nanoencapsulated form of the plant extracts to increase the efficiency of its biological action. So the recent topic based on use of nanoparticals for formulation of antidiabetic herbal drug remedy.[2]

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LITERATURE REVIEW:

The extensive literature survey revealed that herbal drug therapy for diabetes is very targeting now a days & application of nanotechnology definitely improves the pharmacokinetic profile of antidiabetic herbal drugs.

1. **Swarnalatha.L et al (2012)**

   Diabetes is a syndrome which is characterized clinically as hyperglycemia due to absolute or relative deficiency of insulin production and progressive resistance of insulin. In recent years there is a fast increase in the occurrence and prevalence of diabetes mellitus. In the present study *sphaeranthus amaranthoides* was screened for antidiabetic activity invitro. In the present search synthesis of silver phyto nanoparticles and their antidiabetic activity were studied. This is the first attempt of introducing silver herbal nanoparticles isolation and antidiabetic assessment. This is because silver nanoparticles possess a very high surface to volume ratio. This can be utilized in areas where high surface areas are critical for success. This could for example be in the catalytic industry. In biology and biochemistry nanoparticles have attracted much attention. The aim of the current work is to screen for invitro inhibition of alpha-amylase enzyme activity of extract of *sphaeranthus amaranthoides* silver nanoparticles. The silver nanoparticles showed a dose response inhibitory activity on α-amylase. Acarbose was used a standard drug.

2. **Gourav Joshi et al (2011)**

   It is evident from the recent scientific and patent literature that an increased interest in novel dosage forms that are retained in the stomach for a prolonged and predictable period of time exists today in academic and industrial research groups.

3. **P. Saravana Perumal et al (2014)** In the present investigation, administration of alloxan-induced a significant development of diabetic changes that is, fasting blood glucose, bodyweight, food as well as water consumption levels and oxidative stress marker changes that is, TBARS, reduced GSH, as well as NO2− levels in rats. Moreover, treatment of SRE-SD has shown to produce significant attenuating effect on alloxan-induced diabetic and antioxidant changes. Many natural products, especially plants-derived medicines have been promised to treat and management of diabetes mellitus in experimental animal and human trials via antioxidative mechanism. The research report from literature and this study has been revealed that, the S. dulcis has antidiabetic and antioxidant potential. Numerous studies has been reported that herbal constituents such as saponins, tannins, flavonoids, phenolic

compounds, terpenoids, glycosides alkaloids etc., shown to possess the free radical scavenging role in vitro as well as in biological systems and also ameliorated the oxidative injury and disease progress. However, among the all natural compounds, saponins and flavonoids are reported to possess the potential antidiabetic action.

4. **Rinku D. Umrani et al (2014)** This study reveals that Ayurveda recommend Jasada bhasma(zinc based bhasma) as the treatment of choice for diabetes. Interestingly, recent studies suggest that bhasmas comprise submicronic particles or nanoparticles. Thus a bhasma-inspired new drug discovery approach could emerge in which several metal based nanomedicines could be developed. This would help in utilizing the age old, time-tested wisdom of Ayurveda in modern medicine. One such study on antidiabetic activity of Jasada bhasma and the corresponding new drug, namely ,zinc oxide nanoparticles ,is briefly discussed.
5. **Sovan Lal Pal, Utpal Jana et al (2011)** This study shows that there has been an exponential interest in the development of novel drug delivery systems using nanoparticles. Nanoparticles can offer significant advantages over the conventional drug delivery in terms of high stability, high specificity, high drug carrying capacity, ability for controlled release, possibility to use in different route of administration and the capability to deliver both hydrophilic and hydrophobic drug molecules. This review focuses on classification, methods of preparation, characterisation, application, advantages of nanoparticles and health perspectives.
6. **Ebtihal F. Alamoudi et al (2014)** The present study was undertaken to investigate the effect of nanoparticles extracts of *Costus speciosus* on diabetes, because nano-structured systems could promote sustained release of active constituents, reduce the required dose, low toxicity, decrease side effects, and improve activity. The results could be concluded that the nanoparticles of *Costus speciosus* extract increased the potential to be developed as an antidiabetic agent.
7. **Asmita Samadder et al (2014)** This review on diabetes aims to provide information available on research carried out on both traditional and modern medicine practices, highlighting some recent ones including use of nanomedicines that would hopefully be able to give patients a better quality of longer life. This review also focuses on the benefits of using plant products and nanoformulations in reducing side effects and provides convincing evidence of their ameliorative properties.
8. **Mani Rupeshkumar et al (2014)** Herbal medicines have been highly esteemed source of medicine throughout the human history. They are widely used today

indicating that herbs are a growing part of modern high-tech medicine. In recent times, there has been a revived interest within the plant remedies. In this review article an attempt has been made to focus on hypoglycemic plants and may be useful to the health professionals, scientists and scholars working in the field of pharmacology & therapeutics to develop evidence based alternative medicine to cure different kinds of diabetes in man & animals.

9. **V. Ganesh Kumara et al (2011)** This study is Concerning the synthesis of nanoparticles using biological components, the potential applications of biosynthesized nanoparticles as new advanced nanomaterials are currently studied. In this view, the locally available plant with highest antidiabetic potential has been selected in the study to synthesize AuNPsin simple and eco-friendly method.

RATIONALE OF STUDY:

Diabetes is the leading cause of death worldwide after heart disease and as a result there is a pressing need for novel and effective treatments. Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. Despite major breakthroughs in many areas of modern medicine over the past 100 years, the successful control of diabetes remains significant challenge at the start of the 21st century, because it is difficult to discover novel agent that completely prohibit the diabetes. The frequency of administration of dosage forms in diabetes therapy is generally more. So instead of allopathic list of drugs, medicinal plants with proven antidiabetic and related beneficial effects are present. As compare to allopathic drugs herbal drugs shows very less side effect & overdose effect. So now a days herbal remedy for diabetes is the targeting therapy. The use of nanotechnology for herbal drugs is relatively novel approach & it improves the drug efficacy surely.

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PLAN OF WORK:

1. **Literature survey**
2. **Procurement of plant material**
3. **Authentication of plant material**
4. **Extraction**
5. **Preliminary phytochemical evaluation of drugs extract**
6. **Pharmacological evaluations**
   - **Acute Toxicity Study.**
   - **Evaluation of antidiabetic activity**

   # Preliminary study:

   1) Antihyperglycemic study in non-diabetic rats.

   2) Hypoglycemic study in non-diabetic rats.

   # Antidiabetic study:

   Chronic study in Alloxan-induced diabetic rats.
7. **Preparation of nanoparticals of drug extract.**
8. **In vitro evaluation study of nanoparticals.**
9. **Study of improvement in pharmacokinetic profile of antidiabetic polyherbal nanopartical prepation.**

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TENTATIVE DURATION OF WORK

S.N.	ACTIVITY	PERIOD (IN MONTHS)
1	Literature survey	6 Months
2	Collection of Plant material	3 Months
3	Extraction of plant materials	5 Months
4	Phytochemical study	4 Months
5	Evaluation of antidiabetic activity	5 Months
6	Preparation & evaluation of dosage form	9 months
7	Other suggested work and compilation of data	4 Months
	Total duration of project	**36 Months**

RESEARCH OUTCOME

In spite of good advancements for diagnosis and treatment, diabetes is still a big threat to our society. This is the most common disease for maximum deaths in the world & specially in India. So there has been an intense search needed on various biological sources to develop a novel anti-diabetic formulation to combat this disease. Patients who already got crippled with this disease, who are further burdened by drug-induced toxic side effects, have now turned to seek help from the complementary and alternative formulation hoping for a better cure. Plants have proved to be an important natural source of anti-diabetic therapy for several years. Many promising antidiabetic agents are derived from natural products. Current study will investigates promising novel antidiabetic drug delivery system of natural products which may have better pharmacokinetic profile than existing formulations with lesser side effects.

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REFERENCES:

1. Asmita Samadder, Anisur Rahman Khuda-Bukhsh, 2014, "Nanotechnological approaches in diabetes treatment: A new horizon", World J Transl Med 2014 August 12; 3(2): 84-95.
2. Beenish Ehsan , Muhammad Qasim, Mahmmad S Masoud, Mahmood ur Rehman, shah Jahan, Usman Ali Ashfaq , 2013, Therapeutic potential of herbs against diabetes, Pure Appl. Bio., 2(4): 138-147, Dec-2013.
3. Swarnalatha.L*, Christina Rachela, Shruti ranjanb, Payas baradwaj,2012, Evaluation of Invitro Antidiabetic Activity of Sphaeranthus Amaranthoides Silver nanoparticles, International Journal of Nanomaterials and Biostructures,19 July 2012, 2(3) 25-29.
4. Gourav Joshi, Seema Saini, Sandeep Arora,Arvind Sharma, Vikas Kumar,2011, Innovation In Gastroretentive Drug Delivery Systems: Formulations And Techniques For Anti-Diabetic Drugs, International Journal of Advances in Pharmaceutical Research, Vol. 2 / Issue. 4, April 2011, 147- 156
5. P. Saravana Perumal, P. V. Anaswara, A. Muthuraman, S. Krishan,2014, "Therapeutic potency of saponin rich aqueous extract of Scoparia dulcis L. in alloxan induced diabetes in rats"., AYU,www.ayujournal.org,april-june-2014,volm 35,211-216.
6. RinkuD.,Umrani and Kishore M.Paknikar,2014, "Jasada bhasma, a Zinc-Based Ayurvedic Preparation: Contemporary Evidence of Antidiabetic Activity Inspires Development of a Nanomedicine", Hindawi Publishing Corporation Evidence-Based Complementary and Alternative Medicine Volume 2015, Article ID 193156, 9 pages.
7. Sovan Lal Pal, Utpal Jana, P. K. Manna, G. P. Mohanta, R. Manavalan,2011, Nanoparticle: An overview of preparation and characterization, Journal of Applied Pharmaceutical Science 01 (06); 2011: 228-234
8. Ebtihal F. Alamoudi, Wagdy K. B. Khalil, Inas S. Ghaly, Nagwa H. A. Hassan, Ekram S. Ahmed,2014, Nanoparticles from of Costus speciosus Extract Improves the

Antidiabetic and Antilipidemic Effects Against STZ-induced Diabetes Mellitus in Albino Rats, International Journal of Pharmaceutical Sciences Review and Research, , 29(1), November – December 2014; Article No. 52, Pages: 279-288

9. Mani Rupeshkumar, Kunchu Kavitha, Pallab Kanti Haldar,*2014, "ROLE OF HERBAL PLANTS IN THE DIABETES MELLITUS THERAPY: AN OVERVIEW", International Journal Of Applied Pharmaceutics,29 april 2014, Vol 6, Issue 3, 1-3
10. V.Ganesh Kumar,S.Dinesh Gokavarapu,2011, "Facile green synthesis of gold nanoparticles using leaf extract of antidiabetic potent Cassia auriculata", Colloids and Surfaces B: Biointerfaces,Elsevier, 87 (2011) 159– 163.
11. Sachinkumar Patil*, Amulyaratna Behera and Sunit Kumar Sahoo,2013, Antidiabetic drug loaded biodegradable nanoparticles for the management of Diabetes mellitus, 3rd International Conference and Exhibition on Pharmaceutics & Novel Drug Delivery Systems, April 08-10, 2013,Volume 4 Issue 2 Page 167.
12. Sanjukta Duarah, Kunal Pujari, Jyotirmoy Ghosh, and Dhanalekshmi Unnikrishnan*,2015,"Formulation and Evaluation of Metformin Engineered Polymeric Nanoparticles for Biomedical Purpose",Research Journal of Pharmaceutical, Biological and Chemical Sciences, May–June 2015 RJPBCS 6(3) Page No. 1005.
13. Hitesh Verma,*Syam B.P,Yashwant, Harmanpreet S,2013, Herbal Drug Delivery System: A Modern Era Prospective,International journal of current pharmaceutical Review and Research, August-october 2013:4(3):88-101

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